

IN THE CLAIMS:

Please amend the claims to have the status and content indicated in the following listing of claims, wherein any cancellation of claims is made *without prejudice*.

Claim 1 (currently amended): A method of diagnosis of onset of endotoxemia or sepsis ~~due attributable~~ to Gram negative bacterial infection said method comprising monitoring of the degree of AP occupancy of ~~LPS (Lipopolysaccharide)~~ lipopolysaccharide (referenced "LPS" hereinafter) binding sites on alkaline phosphatase in a sample of ~~tissue or fluid derived from~~ from a patient, wherein the degree of ~~AP (Alkaline Phosphatase)~~ occupancy is associated with the presence or absence of Gram negative bacterial infection.

Claim 2 (currently amended): A method according to claim 1, wherein the degree of AP occupancy of LPS binding sites on alkaline phosphatase in the sample is lower than that the degree of occupancy of LPS binding sites on alkaline phosphatase of an equivalent sample type of from an individual free of Gram negative infection.

Claim 3 (currently amended): A method according to claim 1, wherein the degree of AP occupancy of LPS binding sites on alkaline phosphatase ~~in a sample or tissue or fluid derived from a patient~~, is monitored over a period of time, and wherein a decline of the degree of AP occupancy indicates Gram negative bacterial infection.

Claim 4 (currently amended): A method according to claim 1, wherein the fluid is serum and the degree of ~~AP~~ occupancy of LPS binding sites on alkaline phosphatase in the sample is determined and wherein onset of decline in the degree of ~~AP~~ occupancy

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indicates onset of Gram negative bacterial infection.

Claim 5 (currently amended): A method according to claim 1 wherein the degree of AP occupancy of LPS binding sites on alkaline phosphatase ~~may also~~ can additionally indicate a mixed ~~or single~~ infection of Gram negative and Gram positive bacteria.

Claim 6 (currently amended): A method according to claim 1 wherein the method comprises subjecting the sample ~~is subjected~~ to binding with a ligand having affinity for the LPS binding site on alkaline phosphatase followed by ~~a determination of~~ determining the degree of binding of the ligand.

Claim 7 (currently amended): A method according to claim 1 wherein the LPS binding sites are occupied by one or more ligands having affinity for the LPS binding site ~~on alkaline phosphatase is the ligand or ligands being~~ selected from the group consisting of naturally occurring ligands, chemically modified or genetically modified derivatives of natural LPS binding site binding substances, and chemically produced ligands.

Claim 8 (currently amended): A method according to claim 1, wherein the sample is subjected to binding with a ligand having affinity for the LPS binding site on alkaline phosphatase and wherein the ligand is selected from the group consisting of LPS, Lipid A, ~~and~~ LPS binding site antibody against alkaline phosphatase, a Fab fragment with LPS binding site binding ability ~~on~~ with alkaline phosphatase, a single chain fragment of an immunoglobulin having LPS binding site binding activity ~~on with~~ alkaline phosphatase.

Claim 9 (currently amended): A method according to claim ~~7~~ 8, wherein the LPS binding site binding ligand has at least the affinity for the LPS binding site of alkaline phosphatase of LPS

Claim 10 (currently amended): A method according to claim ~~7~~ 8, wherein the LPS binding site binding ligand has at least the affinity for the LPS binding site of alkaline phosphatase of lipid A.

Claim 11 (previously amended): A method according to claim 1 wherein the degree of ~~AP~~ occupancy of LPS binding sites on alkaline phosphatase is determined by assessment of the dephosphorylating capacity of alkaline phosphatase in the sample.

Claim 12 (currently amended): A method according to claim 11, wherein the ratio of dephosphorylating alkaline phosphatase to non-dephosphorylating alkaline phosphatase is determined.

Claim 13 (currently amended): A method according to claim 12, wherein the ratio of dephosphorylating alkaline phosphatase to non-dephosphorylating alkaline phosphatase is determined ~~using the values obtained by~~ assessment of total alkaline phosphatase activity using biochemical methods to determine dephosphorylating activity, ~~and by assessment of total amounts of alkaline phosphatase,~~ optionally using e.g. antibodies or otherwise suitable discriminating entities and by calculating the ratio of these values.

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Claim 14 (currently amended): A method according to claim 1 wherein the sample is from a cholestasis-free patient.

Claim 15 (previously amended): A method according to claim 1 wherein the method also comprises a further assay of a sample from the patient for another disease related to increase of alkaline phosphatase activity, said further assay employing a method avoiding determination of alkaline phosphatase level.

Claim 16 (currently amended): A method according to claim 15 wherein the further assay is carried out when no decline in AP occupancy of LPS binding sites of alkaline phosphatase according to the method of any of claims 1-14 is detected.

Claim 17 (previously amended): A method according to claim 1, wherein the sample is taken from an individual at risk of Gram negative bacterial infection.

Claim 18 (currently amended): A method according to claim 17 wherein the sample is taken from an individual either both prior to and following trauma or shortly after having undergone trauma, wherein the trauma in particular concerns comprises surgery, burns or ischemic traumas.

Claim 19 (previously amended): A method according to claim 1 wherein the sample is taken from an individual during hospitalization.

Claim 20 (currently amended): A method according to claim 1 wherein the sample is

taken a number of times ~~over~~ during a period of time and the data are compared ~~thus~~  
~~revealing to reveal~~ the level of AP degree of alkaline phosphatase binding site  
occupancy over time.

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Claim 21 (currently amended): A method according to claim ~~1~~ 20 wherein the period of  
time is as long as the individual is at risk of infection i.e. during hospitalization or post  
trauma recovery. during illness, injury, pregnancy, hospitalization and post trauma  
recovery

Claim 22 (currently amended): A method according to claim 1 wherein the result of the  
assay is compared to a standard value ~~thus revealing to reveal~~ whether the degree of  
AP occupancy is indicative of endotoxemia or sepsis or the risk ~~thereof~~ of endotoxemia  
or sepsis.

Claim 23 (currently amended): A method according to claim 1 wherein the sample is a  
blood serum sample ~~selected from the group consisting of blood and tissue, said blood~~  
~~sample for example being serum, and the tissue being other than bone and said tissue~~  
~~for example being selected from liver and intestine.~~

Claims 24-35 canceled.

Claim 36 (currently amended) A method ~~or use~~ according to claim 1 wherein the  
~~method is carried out on a~~ sample is selected derived from the group of individuals  
consisting of a patient, an ~~individual~~ patient at risk of Gram negative bacterial infection,

an individual patient prior to or after trauma, ~~an individual during hospitalization and~~  
a hospitalized patient.

Claim 37 (new): A method of diagnosis of onset of endotoxemia or sepsis due to Gram negative bacterial infection the method comprising monitoring alkaline phosphatase activity in a patient blood serum sample to detect a decline of alkaline phosphatase activity indicative of onset of Gram negative bacterial infection.

Claim 38 (new): A method according to claim 37 wherein the decline of serum alkaline phosphatase activity is determined by comparing the result of an assay for alkaline phosphatase activity with an equivalent sample from an individual free of Gram negative infection or with a standard value to indicate whether the decline is indicative of endotoxemia or sepsis or the risk of endotoxemia or sepsis.

Claim 39 (new): A method according to claim 37 wherein multiple alkaline phosphatase activity determinations are made during a period of time and the data are compared to reveal the activity level over time.

Claim 40 (new): A method according to claim 37 wherein the sample is from a cholestasis-free patient or a cholestasis-free patient at risk of Gram negative bacterial infection, a cholestasis-free patient prior to or after trauma, or a hospitalized cholestasis-free patient.

Claim 41 (new): A method according to claim 38 wherein multiple alkaline

phosphatase activity determinations are made during a period of time and the data are compared to reveal the activity level over time and wherein the sample is from a cholestasis-free patient or a cholestasis-free patient at risk of Gram negative bacterial infection, a cholestasis-free patient prior to or after trauma, or a hospitalized cholestasis-free patient.

Claim 42 (new): A method according to claim 41 comprising subjecting the sample to binding with a ligand having affinity for the LPS binding site on alkaline phosphatase followed by determining the degree of binding of the ligand wherein the ligand is selected from the group consisting of LPS, Lipid A, and LPS binding site antibody against alkaline phosphatase, a Fab fragment with LPS binding site binding ability on with alkaline phosphatase, a single chain fragment of an immunoglobulin having LPS binding site binding activity on with alkaline phosphatase.

Claim 43 (new): A method according to claim 42 comprising determining the ratio of dephosphorylating alkaline phosphatase to non-dephosphorylating alkaline phosphatase.

Claim 44 (new): A method according to claim 42 wherein the sample is taken from an individual either both prior to and following trauma or shortly after having undergone trauma, wherein the trauma comprises surgery, burns or ischemic traumas.